Poly(I)- Poly(C12U)

Brand Name: Ampligen
Drug Class: Opportunistic Infection and Other Drugs

Drug Description

Poly(I)-poly (C12U), a specifically mismatched doublestranded RNA (dsRNA) nucleic compound, is a biological response modifier with anti-HIV activity. [1]

HIV/AIDS-Related Uses

Poly(I)-poly(C12U) is in Phase IIb studies for the treatment of HIV as monotherapy or as an addition to failing regimens of highly active antiretroviral therapy (HAART).[2] Poly(I)-poly(C12U) is also being evaluated for its role in lengthening the duration of structured treatment interruptions (STIs) of HAART therapy.[3]

Non-HIV/AIDS-Related Uses

Poly(I)-poly(C12U) has widespread antiviral activity, including activity against West Nile virus and other flaviviruses.[4] Poly(I)-poly(C12U) is also being studied for the treatment of hepatitis B and C infection, renal cell carcinoma, and malignant melanoma. Phase III studies evaluating the drug for treatment of chronic fatigue syndrome have recently been completed as well.[5]

Pharmacology

Poly(I)-poly(C12U) provides broad activity by activating otherwise dormant cellular defenses against viruses and tumors. Specifically, poly(I)-poly(C12U) activates intracellular antiviral mediators 2-5A synthetase/RNase.[6] [7] The drug's cell-mediated immunomodulatory properties produce a delayed hypersensitivity response, which may delay viral rebound during STIs of HAART.[8]

STI is based on the premise that immune function may recover in stable HIV infected patients by temporarily withdrawing HAART, allowing viral rebound to stimulate the immune response. However, efforts to date have produced conflicting results. When given during the interruption period, poly(I)-poly(C12U) appears to stabilize patients and allows a longer duration of interrupted therapy.[9]

In a Phase IIb study of poly(I)-poly(C12U) for treatment of HIV during STI, 22 patients with viral loads below 50 copies/ml and CD4 counts of at least 400 cells/mm3 were randomized to receive poly(I)-poly(C12U) 400 mg IV twice weekly or no treatment during STIs over 64 weeks. STIs continued until the viral load rebounded to at least 5,000 copies/ml for 3 consecutive weeks or 50,000 copies/ml at least once. After 9 months, therapy with poly(I)-poly(C12U) significantly prolonged the duration of STI from a mean 13 weeks without treatment to a mean 27 weeks with the drug. Additionally, the number of CD8 cells significantly increased in patients receiving poly(I)-poly(C12U), destroying additional cells infected with the virus.[10]

During in vitro testing, poly(I)-poly(C12U) was equally active against wild-type and nevirapine-resistant HIV, protease inhibitors, or nucleoside analogue reverse transcriptase inhibitors.[11]

Adverse Events/Toxicity

Poly(I)-poly(C12U) appears generally well tolerated as monotherapy or as concomitant anti-HIV therapy in clinical studies. In a 9-month trial of poly(I)-poly(C12U) in HIV infected patients, adverse effects were primarily mild and self-limiting. To date, lactic acidosis, insulin resistance, and hyperlipidemia have not been noted in relation to poly(I)-poly(C12U) therapy.[12] [13]

Drug and Food Interactions

Poly(I)-poly(C12U) is synergistic with zidovudine in decreasing CD4 counts in patients receiving combination therapy for more than a year. Poly(I)-poly(C12U) also appears to resensitize zidovudine-resistant HIV when given concomitantly.[14] In addition, in vitro studies have demonstrated poly(I)-poly(C12U) synergy with the following antiretroviral medications: abacavir, amprenavir, didanosine, efavirenz, indinavir, ritonavir, nelfinavir, stavudine, zalcitabine, and zidovudine.[15]

Poly(I)- Poly(C12U)

Clinical Trials

For information on clinical trials that involve Poly(I)-Poly(C12U), visit the ClinicalTrials.gov web site at http://www.clinicaltrials.gov. In the Search box, enter: Poly(I)-Poly(C12U) AND HIV Infections.

Dosing Information

Mode of Delivery: Intravenous.[16]

Dosage Form: In clinical trials, poly(I)-poly(C12U) 400 mg is administered intravenously twice weekly.[17] [18]

Chemistry

CAS Name: 5'-Inosinic acid, homopolymer, complex with 5'-cytidylic acid polymer with 5'-uridylic acid (1:1)[19]

CAS Number: 38640-92-5[20]

Molecular formula:

Poly(I)- Poly(C12U)

Chemistry (cont.)

Other Names

Atvogen[22]

AMP[23]

Poly I:poly C12U[24]

Further Reading

Essey RJ, McDougall BR, Robinson WE Jr. Mismatched double-stranded RNA (polyI-polyC(12)U) is synergistic with multiple anti-HIV drugs and is active against drug-sensitive and drug-resistant HIV-1 in vitro.Antiviral Res. 2001 Sep;51(3):189-202. PMID: 114488730

Mismatched double-stranded RNA: polyI:polyC12U. Drugs R D. 2004;5(5):297-304. PMID: 15357629

Safety and Efficacy of Ampligen in the Treament of HIV Patients Failing HAART. Available at:

Poly(I)- Poly(C12U)

Further Reading (cont.)

Poly(I)- Poly(C12U)

Further Reading (cont.)

The Role of Ampligen in Strategic Therapeutic Intervention (STI) of HAART. Available at:

Manufacturer Information

Poly(I)-Poly(C12U)
Hemispherx Biopharma, Inc
One Penn Ctr
1617 JFK Blvd, 6th Floor
Philadelphia, PA 19103
(215) 988-0080

Ampligen
Hemispherx Biopharma, Inc
One Penn Ctr
1617 JFK Blvd, 6th Floor
Philadelphia, PA 19103
(215) 988-0080

For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

• Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET

• Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

Poly(I)- Poly(C12U)

References

1. Intl AIDS Conf - 14th, 2002. Abstract LbPeB9011.

2. Intl AIDS Conf - 14th, 2002. Abstract LbPeB9011.

3. ClinicalTrials.gov - The Role of Ampligen in Strategic Therapeutic Intervention (STI) of HAART. Available at: http://www.clinicaltrials.gov/ct/show/NCT00035893. Accessed 02/24/06.

4. Drugs R D - 2004;5(5):297-304

5. Hemispherx Biopharma, Inc. - Research and Development: Ampligen. Available at: http://www.hemispherx.net/content/rnd/drug_candidates.htm. Accessed 02/24/06.

6. Hemispherx Biopharma, Inc. - Research and Development: Ampligen. Available at: http://www.hemispherx.net/content/rnd/drug_candidates.htm. Accessed 02/24/06.

7. Intl AIDS Conf - 14th, 2002. Abstract LbPeB9011.

8. IAS Conf on HIV Pathogenesis and Treatment - 2nd, 2003. Abstract 596.

9. AEGIS - AIDSWeekly - Treatment Interruption: Ampligen use in HIV treatment show promise [press release], May 19, 2003. Available at: http://www.aegis.com/pubs/aidswkly/2003/aw030508.html. Accessed 02/24/06.

10. IAS Conf on HIV Pathogenesis and Treatment - 2nd, 2003. Abstract 596.

11. Antiviral Res - 2001 Sep;51(3):189-202

12. IAS Conf on HIV Pathogenesis and Treatment - 2nd, 2003; Abstract 596.

13. Eur J Clin Microbiol Infect Dis - 1996 Jul;15(7):580-7

14. In Vivo - 1994 May-Jun;8(3):375-81

15. Antiviral Res - Sep;51(3):189-202

16. Hemispherx Biopharma, Inc. - Research and Development: Ampligen. Available at: http://www.hemispherx.net/content/rnd/drug_candidates.htm. Accessed 02/24/06.

17. Intl AIDS Conf - 14th, 2002; Abstract LbPeB9011.

18. IAS Conf on HIV Pathogenesis and Treatment - 2nd, 2003; Abstract 596.

19. ChemIDplus - Available at: http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp. Accessed 02/24/06.

20. ChemIDplus - Available at: http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp. Accessed 02/24/06.

21. ChemIDplus - Available at: http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp. Accessed 02/24/06.

22. ClinicalTrials.gov - A Study Of Atvogen in Healthy Volunteers and HIV-Infected Patients Who Have No Symptoms of Infection. Available at: http://www.clinicaltrials.gov/ct/show/NCT00001000. Accessed 02/24/06.

23. IAS Conf on HIV Pathogenesis and Treatment - 2nd, 2003; Abstract 596.

24. Int Conf AIDS - 14th, 2002; Abstract LbPeB9011.